

## **Retrospective investigation and analysis of sleep disorders on occurrence of polycystic ovary syndrome.**

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### **Abstract**

**Objective:** To investigate the sleep status before polycystic ovary syndrome (PCOS) and analyze the relationship between sleeping and PCOS.

**Study design:** A retrospective cohort study recruited 129 PCOS patients and 156 non-PCOS infertility women according to Rotterdam criteria. All patients filled in Pittsburgh Sleep Quality Index (PSQI).

**Results:** According to PSQI scoring PCOS patients had a significant sleeping quality score ( $1.24 \pm 0.72$ ) than non-PCOS group ( $0.99 \pm 0.71$ ) ( $P=0.004$ ). The sleeping time score, sleeping disorder score, daytime dysfunction, total score of PSQI and sleep disorders judgment for PCOS group were  $0.71 \pm 0.72$ ,  $1.09 \pm 0.49$ ,  $1.58 \pm 0.77$ ,  $6.82 \pm 2.61$  and 69.77% respectively. There were statistically differences between PCOS group and non-PCOS group. Age and sleep efficiency were identified as protective factors for PCOS, but sleeping disorders, day time dysfunction and snoring were high risk factors for PCOS.

**Conclusion:** Poor sleeping is possible risk for PCOS.

**Keywords:** Polycystic ovary syndrome (PCOS); Sleep disorders; Pittsburgh sleep quality index (PSQI).

*Accepted on June 06, 2016*

### **Introduction**

Polycystic ovary syndrome (PCOS), the most common endocrine disorder among women of reproductive age, affects 5%-10% women [1]. Epidemiological investigation showed that the prevalence rate of PCOS in China is 5.6%. Clinical signs of PCOS include menstrual irregularity, hyperandrogenism and ovarian cysts, which lead to fertility problems, including oligo-anovulation, and infertility. Metabolic disorders related to PCOS include obesity, insulin resistance, gestational diabetes mellitus, diabetes, and cardiovascular disease and so on [2]. For the etiology, it is not clear because its features are heterogeneous. Studies showed that PCOS is strongly heritable and some genes are identified as risks for PCOS [3]. Insulin resistance is also considered to be the main reason for hyperandrogenism and other clinical characteristics of PCOS, and affects approximately 50%-70% of patients [4,5].

Recently, the relationship between PCOS and psychosocial problems has come to the attention of the medical community. Higher risk of mood and anxiety disorders has been reported in women with PCOS. Women with PCOS have higher depression scores and a higher risk of depression independent of body mass index (BMI), which may markedly reduce their quality of life [6,7]. Manizheh Sayyah-Melli et al. reported that

chronic anxiety and depression were the most psychological pattern in PCOS patients. Lower educational level and unemployment were higher in the cases than controls [8]. It suggested that psychological factors are also greatly related to PCOS and are possible inducements. Studies showed women with PCOS have increased sleep disturbances and abnormal sleep architecture [9-11]. Obstructive sleep apnea (OSA) is higher in women with PCOS in comparison to the general population. OSA in women with PCOS exacerbates insulin resistance. These women are prone to develop sleep-disordered breathing (SDB) and metabolic disorders. SDB is an independent risk factor contributing to metabolic dysfunctions in women with PCOS [9,12]. These studies remind that abnormal sleeping is a possible risk of PCOS. In this study, PCOS patients and control patients were enrolled and we retrospectively investigated the sleeping condition of these cases before PCOS and analyzed the relationship between PCOS and sleeping.

### **Materials and Methods**

#### ***Subjects and diagnosed criteria***

Data for this study were obtained from reproductive center of maternal and child health care in Guangdong province during Jan 2015 to June 2015. Women, who attended gynaecological

outpatient clinics, were invited to participate the retrospective cohort study. Patients aged between 23-40 years. The PCOS (129 cases) was diagnosed based on the Rotterdam Criteria. The control group (156 cases) consisted of females aged between 23 and 40 years with regular menstrual cycles and no history of subfertility. PCOS required two out of the following three clinical findings, 1) biochemical hyperandrogenism, 2) polycystic ovaries detected through ultrasound scanning, 3) oligomenorrhea ( $\geq 35$  days between cycles). Women who have additional pathologies related to high androgen, such as congenital adrenal hyperplasia, Cushing syndrome malignancy; testosterone-producing tumours were excluded. Other diseases with ovulation failure, such as hyperprolactinemia, premature ovarian failure and pituitary or hypothalamic amenorrhea were excluded. Thyroid disease, diabetes and participants with psychiatric disorders were also excluded. This study is approved by the Ethics Committee and obtained the signed informed consent from all participants.

### Assessing sleep quality

All participants were asked to complete a validated sleep questionnaire: revised Pittsburgh Sleep Quality Index (PSQI). It has two parts. The first part includes personal information and 7 non PSQI scoring items (the nap time, pre-sleep routine, snoring or not, discomfort, duration time of sleeping disorder before onset of illness, diagnosis of sleeping disorder and the effect of guidance under doctors. The second part includes 19 PSQI scoring items with seven component scores (A-G): subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication

and daytime dysfunction. Each component score is rated from 0, indicating no difficulty, to 3, indicating severe difficulty, and is aggregate to a global score with a maximum difficulty score of 21. A score under 5 indicates good sleep quality. A score above 5 indicates poor sleep quality.

### Statistical analysis

SPSS 13.0 was used to analyze the data. The measurement data were presented as mean  $\pm$  SD. Group differences were evaluated using independent samples t-test. Enumeration data was evaluated using chi-square test. Statistical significance was set at  $P < 0.05$ . To exclude the effect of diet imbalance, environmental pollution and mental stress, logistic regression analysis was used to analyze the effect on sleeping quality.

## Results

### The demographic characteristics of PCOS group and non-PCOS group

The age, height, weight six month ago, educational background, career, BMI and judgment of sleep disorders were shown in Table 1. The height of PCOS group and non-PCOS group was  $158.6 \pm 4.7$  cm and  $158.2 \pm 4.7$  cm respectively; Weight six month ago of PCOS group and non-PCOS group was  $56.1 \pm 9.0$  kg and  $54.4 \pm 8.2$  kg. There was no significance of height, weight six month ago, educational background, career, BMI between PCOS group and non-PCOS group ( $P > 0.05$ ). Age was significantly different between PCOS group and non-PCOS group ( $P < 0.01$ ).

**Table 1.** The demographic characteristics of PCOS group and non-PCOS group [case (%)].

		PCOS group (N=129)	Non-PCOS group (N=156)	$\chi^2$	T value	P value
Age	-	29.03 $\pm$ 3.26	31.72 $\pm$ 3.86	-	-6.365	<0.001*
Height (cm)	-	158.57 $\pm$ 4.73	158.22 $\pm$ 4.73	-	0.621	0.535
Weight six month ago (kg)	-	56.07 $\pm$ 9.03	54.44 $\pm$ 8.15	-	1.608	0.109
Educational background	Primary school	5 (3.88%)	15 (9.62%)	6.961	-	0.138
	Middle school	52 (40.31%)	73 (46.79%)			
	High school	24 (18.60%)	27 (17.31%)			
	Bachelor	46 (35.66%)	40 (25.64%)			
	Master	2 (1.55%)	1 (0.64%)			
Career	Staff	26 (20.16%)	20 (12.82%)	6.234	-	0.397
	Professionals	8 (6.20%)	11 (7.05%)			
	Service personnel	41 (31.78%)	43 (27.56%)			
	Farmer	3 (2.33%)	6 (3.85%)			
	Manual worker	7 (5.43%)	7 (4.49%)			

	Unemployed	36 (27.90%)	51 (32.69%)		
	Freelancer	8 (6.20%)	18 (11.54%)		
BMI (kg/m <sup>2</sup> )	<18.5	12 (9.30%)	21 (13.46%)	1.248	0.742
	18.5-24.0	81 (62.79%)	95 (60.90%)		
	24.0-28.0	23 (17.83%)	25 (16.02%)		
	≥28	13 (10.08%)	15 (9.62%)		

**The non-PSQI and PSQI scoring for PCOS group and non-PCOS group**

Non PSQI scoring, total PSQI scoring and judgment were shown in Table 2. The time for falling asleep was 1.33 ± 0.79 and 1.17 ± 0.85 for PCOS group and non-PCOS group respectively. The score of sleeping efficiency was 0.87 ± 0.83 and 1.01 ± 0.78. The score of sleep medication was 0.05 ± 0.36 and 0.01 ± 0.11. There was no significant difference between the two groups (P>0.05). The score of sleeping quality (P=0.004), the time of sleeping (P=0.022), sleeping disorder (P=0.016), daytime dysfunction (P<0.0001), total PSQI (P<0.0001) judgment for sleeping disorder (P=0.001) have significant difference.

**Table 2:** The non-PSQI and PSQI scoring for PCOS group and non-PCOS group.

	PCOS group (N=129)	Non-PCOS group (N=156)	T value	χ <sup>2</sup>	P value
Sleeping quality (0-3)	1.24 ± 0.72	0.99 ± 0.71	2.9	-	0.004**
The time for falling asleep (0-3)	1.33 ± 0.79	1.17 ± 0.85	1.63	-	0.104
Sleeping efficiency (0-3)	0.87 ± 0.83	1.01 ± 0.78	-1.44	-	0.151

**Table 3.** Single factor logistic regression analysis of PCOS.

Factors	Detail	β value	P value	OR	95% CI
Age	-	-0.227	0	0.797	0.730-0.870
Height	-	-0.052	0.122	0.949	0.888-1.014
Weight	-	0.027	0.07	1.028	0.998-1.059
BMI	<18.5=1	0.983	0.096	2.672	0.841-8.490
	18.5-24.0=2	0.357	0.391	1.429	0.633-3.227
	24.0-28.0=3	-0.053	0.918	0.948	0.342-2.626
	≥ 28.0=4		0.295		
Educational background	Primary school=1	-2.767	0.096	0.063	0.002-1.631
	Middle school=2	-2.093	0.177	0.123	0.006-2.580
	High school=3	-1.925	0.218	0.146	0.007-3.112

Hypnotic time (0-3)	0.05 ± 0.36	0.01 ± 0.11	1.26	-	0.211
Sleeping time (0-3)	0.71 ± 0.72	0.52 ± 0.70	2.31	-	0.022*
Sleeping disorder (0-3)	1.09 ± 0.49	0.95 ± 0.51	2.43	-	0.016*
Daytime dysfunction (0-3)	1.58 ± 0.77	1.12 ± 0.73	5.14	-	<0.001**
Total score of PSQI (0-21)	6.82 ± 2.61	5.74 ± 2.74	3.38	-	<0.001**
Judgment for sleeping disorder (>5)	90 (69.77%)	77 (49.36%)	-	12.2	0.001

**Logistic regression analysis of PCOS**

We conducted single factor logistic regression analysis for 16 factors in questionnaires (Table 3). There was significant difference in sleeping efficiency, daytime dysfunction and snoring or not. With one unit increase of age, the risk for PCOS fall 0.797 folds (P<0.01). The Odds Ratio (OR) of sleeping efficiency was 0.527 (P<0.05). The OR of daytime dysfunction was 1.9 and the OR of snoring was 2.048.

	Bachelor =4	-1.729	0.259	0.177	0.009-3.580
	Master=5		0.438		
Career	Staff=1	0.658	0.29	1.931	0.571-6.525
	Professionals=2	0.35	0.644	1.418	0.322-6.242
	Service personnel=3	0.366	0.513	1.442	0.481-4.324
	Farmer=4	0.338	0.744	1.401	0.184-10.651
	Manual worker=5	1.005	0.239	2.731	0.512-14.567
	Unemployed=6	0.367	0.517	1.443	0.476-4.374
	Staff=7	-0.003	0.924		
The time for falling asleep					
	-	0.402	0.99	0.997	0.649-1.533
Sleeping time	-	-0.64	0.124	1.495	0.895-2.498
Sleeping efficiency	-	0.002	0.006	0.527	0.333-0.835
Sleeping quality	-	0.025	0.992	1.002	0.609-1.650
Sleeping disorders	-	0.151	0.947	1.025	0.497-2.115
Hypnotic medicine	No=0	0.642	0.896	1.163	0.121-11.155
	Yes=1				
Daytime dysfunction	-	0.878	0.01	1.9	1.163-3.105
Judgment for sleeping disorder	"PSQI scoring ≤ 5"=0	-0.008	0.051	2.406	0.996-5.811
	"PSQI scoring>5"=1				
nap time	-	0.717	0.958	0.992	0.743-1.324
Snoring	No=0	13.394	0.028	2.048	1.082-3.877
	Yes=1				

We also conducted multiple factor logistic regression analysis for 16 factors in questionnaires (Table 4). Age worked as covariant. Sleeping efficiency, judgment for sleeping disorders, daytime dysfunction and snoring worked as independent variable factors. The data showed that there was significant difference in PSQI score (>5), daytime dysfunction and snoring. The OR was 2.913, 6.405 and 2.048 respectively, reminding that the three factors are risk factors for PCOS.

**Table 4.** Multiple factor logistic regression analysis of PCOS.

Covariant	β value	P value	OR	95% CI
Intercept	-6.816	0	-	-
Age	0.22	0	1.246	1.150-1.349
Sleeping efficiency score=0	-1.175	0.097	0.309	0.077-1.236
Sleeping efficiency score =1	-0.241	0.719	0.786	0.211-2.922

Sleeping efficiency score =2	-0.133	0.853	0.876	0.215-3.573
Sleeping efficiency score =3	0b	-	-	-
PSQI score ≤ 5	1.069	0.003	2.913	1.426-5.949
PSQI score>5	0b	-	-	-
Daytime dysfunction=0	1.857	0.016	6.405	1.417-28.960
Daytime dysfunction =1	1.139	0.062	3.123	0.944-10.332
Daytime dysfunction =2	0.785	0.2	2.192	0.660-7.280
Daytime dysfunction =3	0b	-	-	-
No snoring	0.669	0.028	1.951	1.076-3.540
Snoring	0b	-	-	-

## Discussion

Studies showed women with PCOS have increased sleep disturbances [9] and abnormal sleep architecture. However no study was conducted to investigate whether poor sleeping is a risk factor for PCOS. In this study, we analysed the relationship between sleeping and PCOS according to revised Pittsburgh Sleep Quality Index. We found that age; sleeping quality, the time of sleeping, sleeping disorder; daytime dysfunction and total PSQI judgment for sleeping disorder were related to PCOS. Age and sleeping efficiency were protective factors of PCOS, but PSQI score (>5), daytime dysfunction and snoring were risk factors. As the most common endocrine disorder, polycystic ovary syndrome (PCOS), affect the fertility and living quality of women of reproductive age [1]. Various causes contributed to it. Insulin resistance and other related mechanism were widely explored [3]. In fact, social psychological factors are greatly related to it. PCOS patients have great stress; meanwhile, stress is also a risk factor for PCOS. Obstructive sleep apnoea syndrome (OSAS) has high cardiovascular risk [13]. Recent studies showed that obstructive sleep apnea was also higher in women with PCOS in comparison to the general population. PCOS women also had significantly reduced sleep quality compared with the controls. In this study, we analyse the he age, height, weight six month ago, educational background, career, BMI and judgment of sleep disorders of POCS and non-PCOS, we found that age is a significant factor. Single factor logistic regression analysis showed that the increase of age protect women from PCOS. Sleeping efficiency had a lower OR. These data imply age and sleeping efficiency were protective factors. The OR of daytime dysfunction and snoring was increased, which indicated that they were risk factors. We also found that sleeping quality, the time of sleeping; sleeping disorder, daytime dysfunction, total PSQI, judgment for sleeping disorder can reflect the poor sleep. These factors have significant differences between PCOS and non-PCOS. Further logistic regression analysis showed that the OR of PSQI, daytime dysfunction and snoring increased, suggesting that they are risk factors of PCOS. The study was a retrospective investigation and it had its limitation, such as small sample sizes and selection bias. Further studies should be done to confirm it.

## Conclusion

In conclusion, poor sleep is a risk factor of PCOS. We should pay more attention to the social psychological health and sleeping of women of reproductive age.

## References

1. Wahl SC. Septic shock--how to detect it early (continuing education credit). *Nursing* 1989; 19: 52-60.
2. Baldani DP, Skrgatic L, Ougouag R. Polycystic Ovary Syndrome: Important Underrecognised Cardiometabolic

- Risk Factor in Reproductive-Age Women. *Int J Endocrinol* 2015; 2015: 786362.
3. Welt CK, Duran JM. Genetics of polycystic ovary syndrome. *Semin Reprod Med* 2014; 32: 177-182.
4. Huang X, Wang P, Tal R, Lv F, Li Y, Zhang X. A systematic review and meta-analysis of metformin among patients with polycystic ovary syndrome undergoing assisted reproductive technology procedures. *Int J Gynaecol Obstet* 2015; 131: 111-116.
5. Domon H, Fujisawa M, Fukazawa T, Morioka N, Kikuchi K, Honda F, Ishibashi K. A case of mandibular dysfunction recovered by EMG-biofeedback therapy. *Nihon Hotetsu Shika Gakkai Zasshi* 1988; 32: 396-402.
6. Dokras A. Mood and anxiety disorders in women with PCOS. *Steroids* 2012; 77: 338-341.
7. Dokras A, Clifton S, Futterweit W, Wild R. Increased prevalence of anxiety symptoms in women with polycystic ovary syndrome: systematic review and meta-analysis. *Fertil Steril* 2012; 97: e222.
8. Sayyah-Melli M, Alizadeh M, Pourafkary N, Ouladsahebmadarek E, Jafari-Shobeiri M, Abbassi J, Kazemi-Shishvan MA, Sedaghat K. Psychosocial Factors Associated with Polycystic Ovary Syndrome: a Case Control Study. *J Caring Sci* 2015; 4: 225-231.
9. Vgontzas AN, Legro RS, Bixler EO, Grayev A, Kales A, Chrousos GP. Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance. *J Clin Endocrinol Metab* 2001; 86: 517-520.
10. Zanisi M, Messi E. Sex steroids and the control of LHRH secretion. *J Steroid Biochem Mol Biol* 1991; 40: 155-163.
11. Shreeve N, Cagampang F, Sadek K, Tolhurst M, Houldey A, Hill CM, Brook N, Macklon N, Cheong Y. Poor sleep in PCOS; is melatonin the culprit? *Hum Reprod* 2013; 28: 1348-1353.
12. Chatterjee B, Suri J, Suri JC, Mittal P, Adhikari T. Impact of sleep-disordered breathing on metabolic dysfunctions in patients with polycystic ovary syndrome. *Sleep Med* 2014; 15: 1547-1553.
13. Ciccone MM, Favale S, Scicchitano P, Mangini F, Mitacchione G, Gadaleta F, Longo D, Iacoviello M, Forleo C, Quistelli G, Taddei S, Resta O, Carratù P. Reversibility of the endothelial dysfunction after CPAP therapy in OSAS patients. *Int J Cardiol.* 2012; 158: 383-386.

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